American Journal of Medical Genetics 68:50–53 (1997)

Brief Clinical Report

Mosaic Partial Trisomy 17 Due to a Ring Chromosome Identified by Fluorescence In Situ Hybridisation

P.J. Morrison,* N.M. Smith, K.E. Martin, and I.D. Young
Centre for Medical Genetics, City Hospital, Nottingham, United Kingdom

We report on a 3-year-old-girl with mosaic partial trisomy 17 due to an additional ring chromosome 17 in 13% of cells analysed. This was identified by fluorescence in situ hybridisation (FISH) using a whole chromosome 17 specific paint as well as probes specific for the Smith-Magenis and Miller-Dieker regions of chromosome 17p. This girl showed mild developmental delay with subtle facial and other minor abnormalities including single palmar creases, generalised joint laxity, and a scoliosis. Am. J. Med. Genet. 68:50–53, 1997

KEY WORDS: mosaic partial trisomy 17; ring chromosome 17; FISH

INTRODUCTION

Partial trisomy involving both the short and long arms of chromosome 17 is extremely rare. Ring chromosome 17 is also rare having been identified in only a few children, almost half of whom have presented with Miller-Dieker syndrome [Teyssier et al, 1992]. In most cases of ring 17 the ring chromosome has replaced a normal number 17 chromosome resulting in monosomy for the deleted distal portions of each arm. We now report the clinical findings in a young girl with partial trisomy 17 due to mosaicism for an additional ring 17 chromosome.

CLINICAL REPORT

The 3-year-old proposita is the first and only child of healthy unrelated parents. Her father and mother were 24 and 22 years old, respectively, at the time of her delivery. Following an uneventful pregnancy, she was born at term by Caesarian section because of breech presentation. Birth weight was 3.6 kg. During the neonatal period there were feeding difficulties and bilateral dislocation of the hips was noted. This responded well to conventional treatment with splints. Otherwise general health in infancy was good.

Concern first arose because of mild delay in acquisition of verbal skills at around 2 years. Formal hearing evaluation showed no abnormality. On recent assessment she had a limited vocabulary of 20–30 words and could not use two word sentences. Motor and social skills also showed mild delay. No major behaviour problems were noted. On physical examination, head circumference and length fell on the 2nd and 50th centiles, respectively. She also had folded helices, deep-set eyes, thin upper lip, full lower lip, macroglossia, macrostomia, and maxillary hypoplasia (Fig. 1), bilateral single transverse palmar creases, discrepancy in hand size with the right hand being smaller than the left, long narrow feet, generalised joint laxity, and a scoliosis. Spinal roentgenograms showed no underlying structural abnormality. The child showed no evidence of abnormal or differential pigmentation.

Cytogenetic studies performed on peripheral blood lymphocytes using standard Giemsa banding at 550 band resolution revealed an additional marker chromosome in 13% (6 out of 45) of cells examined (Fig. 2). Further analysis confirmed this to be a small ring chromosome, which was silver stain negative. C-banding showed this to be centric with most of the material being euchromatic (C-band negative). Fluorescence in situ hybridisation (FISH) studies using a whole chromosome 17 specific paint (CAMBIO) indicated that the ring was of chromosome 17 origin (Fig. 3). FISH using DNA probes specific for the Smith-Magenis (D17S29, from ONCOR) and Miller-Dieker (D17S379 from ONCOR) regions of 17p showed a signal on the ring chromosome when hybridised with the former but not with the latter probe (Fig. 4). An alternative explanation would be that the signal seen in the ring chromosomes derived from the RARA component of the ONCOR Smith-Magenis probe. However in view of the proximity of this signal to the centromere, it is more

*Correspondence to: Dr. Patrick J. Morrison, Department of Medical Genetics, Belfast City Hospital, Lisburn Road, Belfast, BT9 7AB, Northern Ireland.

Received 15 November 1995; Accepted 6 March 1996

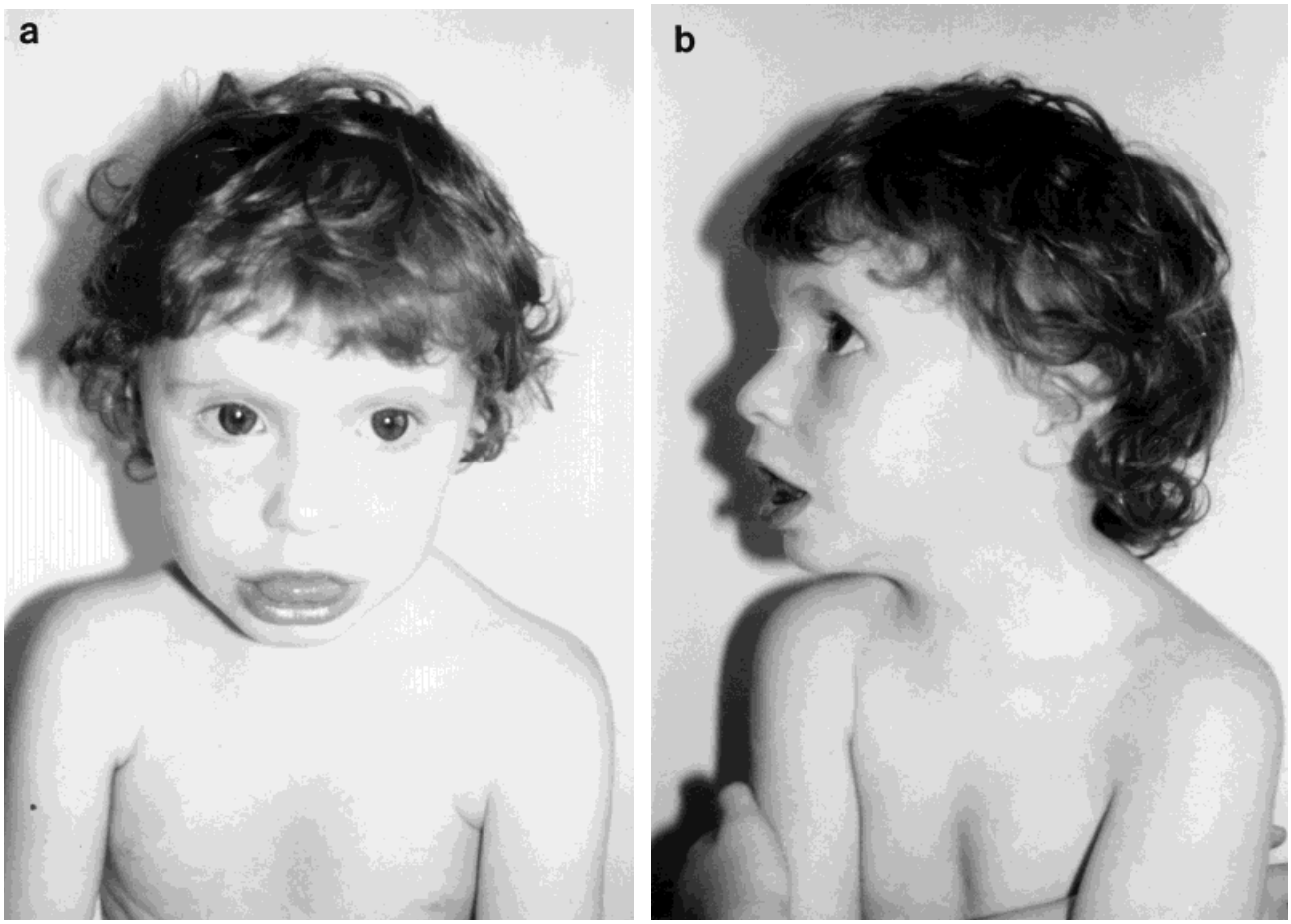

Fig. 1. **a,b**: Facial views of the proposita at age 3 years.

Fig. 2. G banded metaphase spread from the proband showing the additional ring chromosome (arrow).

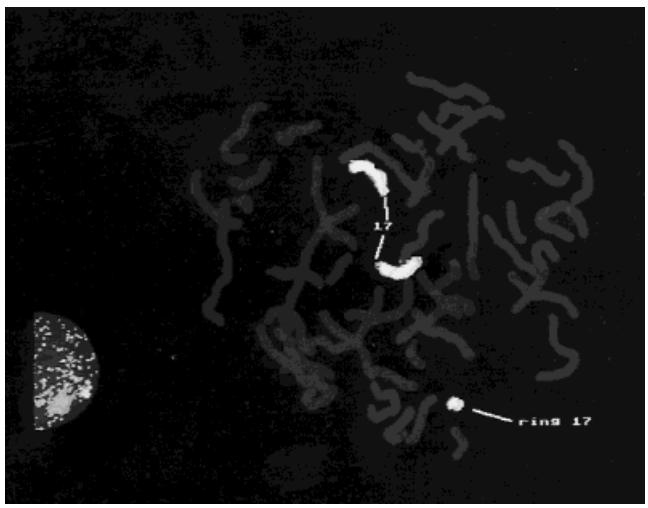

Fig. 3. Metaphase spread hybridised with a whole chromosome 17 specific paint (CAMBIO).

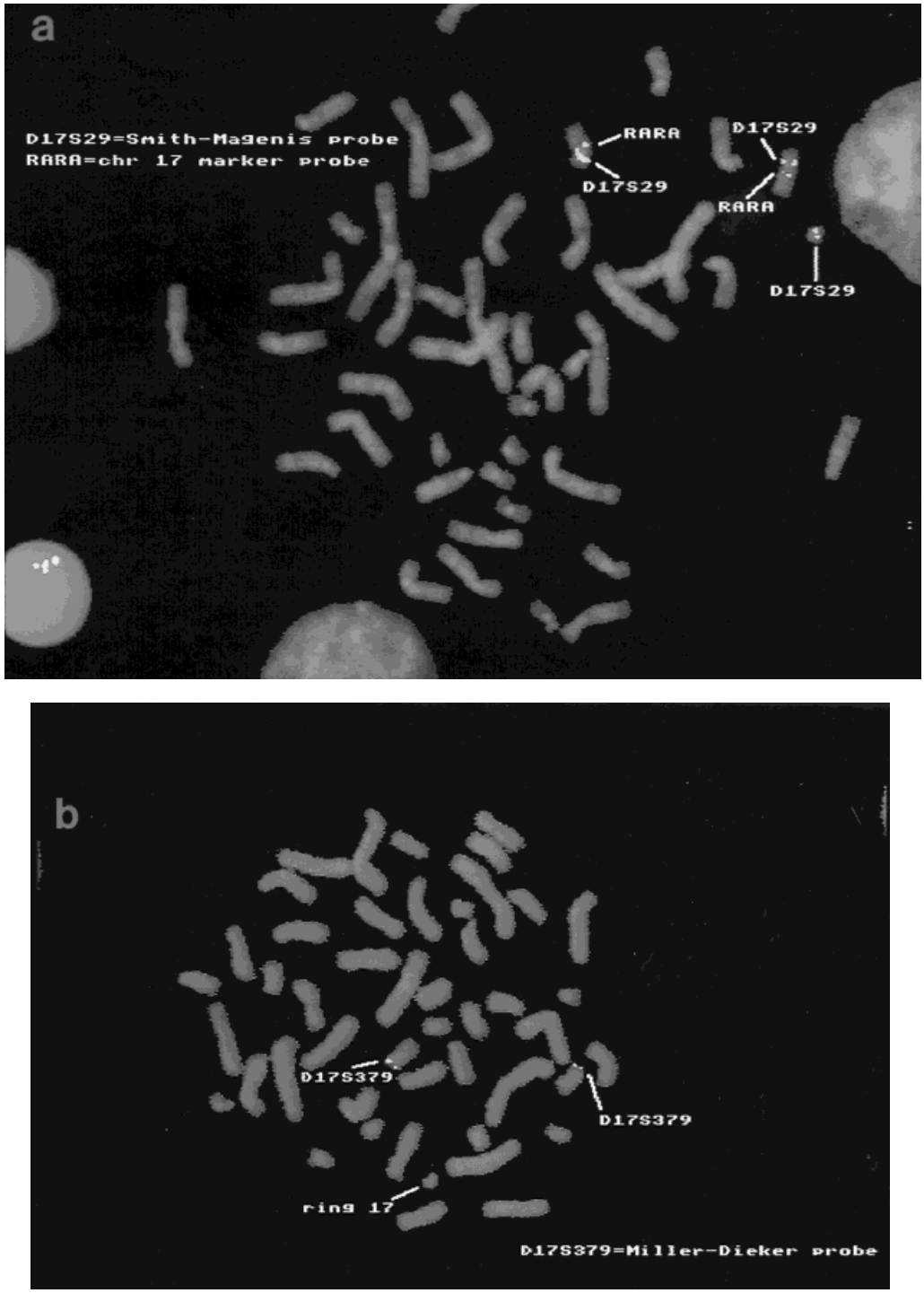

Fig. 4. **a,b**: Metaphase spread hybridised with probes specific for a) the Smith-Magenis (signal present) and b) the Miller-Dieker (signal absent) regions.

likely to be from D17S29 (ie the Smith-Magenis probe). This, therefore, exludes the Miller-Dieker region of 17p13.3 and includes the Smith-Magenis region of 17p11.2. The karyotype was formally reported as 46,XX/47,XX,+r(17)(p12q11).fish r(17)(wcp17+,D17S29+, D17S379-) (ISCN 1995). Parental chromosome studies showed no abnormality in all 30 cells analysed from each parent.

DISCUSSION

The development of FISH has facilitated the identification of additional marker and ring chromosomes

detected prenatally. This in turn has focused attention on the relative lack of information that is presently available about the long-term prognosis for development in such children. While it is recognised that duplication of 17p [Spinner et al., 1993], proximal 17q [Butt et al., 1993] and distal 17q [Turleau et al., 1979] each cause severe retardation and structural abnormalities, information about the clinical consequences of an additional ring 17 chromosome is extremely limited.

Wiktor et al. [1992] reported a 13-year-old girl who had a complex karyotype with four cell lines, i.e., normal, + ring (17), + ring (X), and + ring (17) + ring (X). This girl showed only mild retardation with minor facial and other anomalies. Rosenberg et al. [1995] recently described a 15-year-old girl with a 46, XX (6%), 47, XX+r (17) (94%) karyotype. This girl also showed mild retardation with short stature and minor anomalies. Our patient is the third to be reported with a confirmed additional ring 17. She shares with the other two patients mild developmental delay and only minor structural abnormalities.

The findings in these three patients suggest that the long-term outlook for children who are mosaic for an additional ring 17 chromosome is not necessarily as gloomy as might be expected, although obviously counselling will be influenced by the size of the ring and the proportion of cells in which it is present.

An additional point that should be remembered when counselling prospective parents of a child with an additional ring 17 chromosome is that there is a significant possibility that duplication of 17p11.2-p12 will lead to the clinical manifestation of Charcot-Marie-Tooth disease type 1A in adult life [Chance et al., 1992; Lupski et al., 1992]. At present our patient shows no clinical features of Charcot-Marie-Tooth disease but this is not surprising in view of her youth and the relatively low degree of mosaicism identified in lymphocytes. We feel that it would be unethical to subject this child to nerve conduction studies at such a young age but recognise that neurological assessment in adult life could help clarify the proportion of cells in which the duplication has to be present for neurological abnormalities to become manifest.

REFERENCES

Butt AM, Mehta D, Goodeve JA, Flinter FA (1993): Probable de novo 17q duplication (q11.2 → q21.1): A newly recognised chromosomal syndrome in a child with Klinefelter's syndrome. J Med Genet 30: 436–437.

Chance PF, Bird TD, Matsunami N, Lensch MW, Brothman AR, Feldman GM (1992): Trisomy 17p associated with Charcot-Marie-Tooth neuropathy type 1A phenotype. Neurology 42:2295–2299.

Lupski JR, Wise CA, Kuwano A, Pentao L, Parke JT, Glaze DG, Ledbetter DH, Greenberg F, Patel PI (1992): Gene dosage is a mechanism for Charcot-Marie-Tooth disease type 1A. Nat Genetics 1:29–33.

Rosenberg C, Borovik CL, Canonaco RS, Sichero LC, Queiroz APS, Vianna-Morgante AM (1995): Identification of a supernumerary marker derived from chromosome 17 using FISH. Am J Med Genet 59:33–35.

Spinner NB, Biegel JA, Sovinsky L, McDonald-McGinn D, Rehberg K, Parmiter AH, Zackai E (1993): 46,XX,15p+ documented as dup (17p) by fluorescence in situ hybridisation. Am J Med Genet 46: 95–97.

Teyssier M, Charrin C, Corgiolu Theuil G, David L (1992): Ring chromosome 17: Case report and review of the literature. Ann Genet 35:75–78.

Turleau C, De Grouchy J, Bouveret JP (1979): Distal trisomy 17q. Clin Genet 16:54–57.

Wiktor A, Van Dyke DL, Weiss L (1992): Characterisation of a de novo 48,XX,+r(X), +r(17) by in situ hybridisation in a patient with neurofibromatosis (NF1). Am J Med Genet 45:22–24.